

Applicants: Pinsky et al.  
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claims to show the changes made herein relative to the previous version of the claims.

**Rejection under 35 U.S.C. §112, First Paragraph**

The Examiner rejected claims 1, 3, 5, 7 and 9-27 under 35 U.S.C. §112, first paragraph, because the specification allegedly does not enable a person skilled in the relevant art to use the invention commensurate in scope with the claims. Applicants understand the Examiner's rejection of claims 1, 3, 5, 7 and 9-15 to apply to new claims 28-36 corresponding thereto. Applicants also note that claim 17 has been canceled.

In response to the rejection of new claims 28-36, applicants respectfully traverse.

New claims 28-36 provide a method for reducing ischemic damage to tissue being transplanted into a subject, which comprises contacting the cells of the tissue with an inhibitor of Early Growth Response Factor-1 (Egr-1) ex vivo prior to the tissue's transplantation into the subject.

Applicants maintain that the specification enables the method of new claims 28-36 such that one skilled in the relevant art can practice the claimed method without undue experimentation. Specifically, applicants note that the reduction of ischemic damage is accomplished through ex vivo (i.e., direct) contact with Egr-1 inhibitor, thereby overcoming certain obstacles to delivery which

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may be encountered during *in vivo* administration, depending on the tissue in question. To underscore their position that the instant method is enabled, applicants direct the Examiner's attention to page 53, line 16 to page 57, line 29 of the specification, clearly showing successful Egr-1 suppression in an isogenic rat lung transplant model system.

In response to the rejection of claims 16 and 18-27, applicants respectfully traverse.

Claims 16 and 18-27 provide a method for reducing vascular injury during reperfusion of an ischemic tissue in a subject which comprises contacting the vascular tissue within the ischemic tissue with a compound which inhibits expression of Early Growth Response Factor-1 (Egr-1) protein in the vascular tissue so as to reduce vascular injury in the ischemic tissue during reperfusion.

Applicants maintain that the specification enables claims 16 and 18-27 such that one skilled in the relevant art can practice the claimed method without undue experimentation.

Specifically, applicants note that the tissue being contacted with the compound is *vascular*, and that vascular tissue can be directly and readily contacted with a compound upon intravenous administration of that compound to a subject. The therapeutic effect of such administration is a systemic one - i.e., the treatment of the vascular *system*. Underscoring this point, the Examiner cites U.S. Patent No. 5,593,974, which states that

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"[w]here the intended therapeutic effect is a systemic one, oligonucleotides may be administered systemically."

Applicants maintain that because claims 16 and 18-27 provide for the *systemic* administration of a compound to reduce *vascular* injury, undue experimentation would not be required to practice the claimed methods.

In view of the above remarks, applicants maintain that claims 16 and 18-36 and satisfy the requirements of 35 U.S.C. §112, first paragraph.

**Rejection under 35 U.S.C. §112, Second Paragraph**

The Examiner also rejected claims 1, 3, 5, 7 and 9-27 as allegedly indefinite for failing to point out and distinctly claim the subject matter which applicants regard as the invention. Applicants understand the rejection of canceled claims 1, 3, 5, 7, and 9-15 to apply to new claims 28-36 corresponding thereto.

Specifically, the Examiner alleges that the term "ischemic tissue" recited in the claims is a relative term that renders the claims indefinite, and that one skilled in the relevant art would not be reasonably apprised of the scope of the invention.

In response, applicants respectfully traverse the Examiner's rejection. Applicants maintain that the term "ischemic" is well known in the relevant art. In support of their position,

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applicants attach hereto as **Exhibit B** a copy of page 505 of the Concise Dictionary of Biomedicine and Molecular Biology, which defines "ischemia" as "[i]nadequate blood flow in the tissue characterized by pain and organ dysfunction." Applicants maintain that the term "ischemic tissue", i.e., tissue having, or which has had, inadequate blood flow therein and which is characterized by the dysfunction resulting from such inadequate blood flow, is not indefinite and that those skilled in the relevant art would be reasonably apprised of the scope of the invention.

In view of the above remarks, applicants maintain that claims 16 and 18-36 satisfy the provisions of 35 U.S.C. §112, second paragraph.

#### **Summary**

In view of the remarks made herein, applicants maintain that the claims pending in this application are in condition for allowance. Accordingly, allowance is respectfully requested.

If a telephone interview would be of assistance in advancing the prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

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No fee is deemed necessary in connection with the filing of this Amendment. However, if any fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to:  
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Washington, D.C. 20231.  
Box AF

Alan J. Morrison  
Reg. No. 37,399

Date

4/5/03

Marked-up Version of the Claims

Additions to the text are indicated by underlining; deletions are indicated by square brackets.

16. (Amended) A method for reducing vascular injury during reperfusion of an ischemic tissue in a subject which comprises contacting the vascular tissue within the ischemic tissue with a compound which inhibits expression of Early Growth Response Factor-1 (Egr-1) protein in the vascular tissue so as to reduce vascular injury in the ischemic tissue during reperfusion.
18. (Amended) The method of claim 16, wherein the ischemic tissue is an organ to be transplanted into the subject.
19. (Amended) The method of claim 16, wherein the ischemic tissue is part of a lung, a heart, a kidney, a vein, an artery, a stomach, a colon, a liver, skin, an eye, a pancreas, a brain, a finger, a toe or a limb.
25. (Amended) The method of claim 16, wherein the vascular injury comprises cell death, abnormal cell function, abnormal cell growth, or inability of a [for] cell to maintain normal function.
27. (Amended) The method of claim 16, wherein the inhibitor is contacted with the vascular tissue before, during, or after reperfusion of the ischemic tissue.